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Laboratory **ANALYSIS**

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Rheology & Texture of Pharmaceutical and Cosmetic *Semi*SOLIDS

Rheological measurements can help formulate products and improve processing efficiency.

RHEOLOGY IS THE STUDY OF THE FLOW AND DEFORMATION of materials. Rheological instrumentation and measurements have become essential tools in company's analytical laboratories because they can characterize ingredients and final products and also predict product performance and consumer acceptance.

The materials under investigation can include low-viscosity fluids, semisolids and gels, and hard, solid-like products. A knowledge of rheological and mechanical properties is key in designing flow processes for production and quality control, predicting storage stability, and in understanding and controlling texture. Quality attributes such as lubricity and body affect the acceptance of semisolid products by the end user.

Semisolid products are the most difficult to characterize rheologically because they combine both liquid and solid properties. Many pharmaceutical materials are semisolids such as ointments, creams, pastes and gels. Pharmaceutical and cosmetic processes such as new ingredient selection, formulation preparations, material packaging and shelf storage are all associated with a complex material flow.

Since application and acceptance of pharmaceuticals and cosmetics depends on the flow properties of the final product, rheological measurements can help scientists formulate optimal pharmaceutical and cosmetic products and improve processing efficiency.

Rheological Instrumentation

Scientists consider rheological instrumentation a required analytical tool and they use it on a daily basis. These research-grade instruments are Windows-based and measurements are made quickly with straightforward, user-friendly software. The operator simply loads the sample into the instrument, selects the appropriate experiment and the instrument does the rest.

Pharmaceutical semisolids typically consist of a number of components mixed to produce a desired texture profile or finished product. These materials exhibit a wide range of material response. Depending on the test conditions, their behavior can range from liquid-like to solid-like. Traditionally, single-point viscosity tests have been performed using empirical techniques. But these experiments compress the complex viscoelastic response into a single parameter and do not adequately characterize or provide insight into the full rheological profile of these materials.

The materials in use today are slated for specific applications and, as a result, their cost is high. Detailed knowledge and an objective, reproducible, multipoint measurement capable of decomposing the rheological behavior into individual viscous and elastic components is necessary. Both the DYNALYSER, a rheological characterization system, and the STRESSTECH HR Rheometer (ATS RheoSystems/REOLOGICA Instruments AB) used in this study provide all of the required instrument features and capabilities.

The DYNALYSER and the STRESSTECH HR are analytical instruments capable of measuring viscous, elastic and viscoelastic properties of liquids, gels and solids. Both instruments provide a broad measurement range, from low-viscosity samples such as UV curable monomers; viscous products such as two-component epoxy systems, gels and prepregs; to rigid, solid-state samples.

Steady Shear, Viscosity Analyzed

Two cosmetic creams, one showing good and one showing poor storage stability were analyzed using the STRESSTECH Rheometer. Both samples were characterized using a 40-mm parallel plate measuring system with a gap of 1.0 mm. Cosmetic creams are complex dispersions of solid and liquid particles in which the dispersed particles interact and form a weakly aggregated structure. The viscosity for the samples was obtained in a continuous ramp of stress from 10-3 to 100 Pa in 100 seconds at room temperature (Fig. 1).

Three basic elements of these results are important. The first is the limiting value in viscosity for the two materials. Note that sample B has a higher viscosity (700 Pa_s) than sample A (400 Pa_s) at low stresses. The second important parameter is the critical stress range at which the viscosity starts to decrease. In the range of 1-5 Pa, both samples show a pronounced decrease in viscosity. The third important feature of these results is the rate at which the viscosity decreases above the critical stress, or the slope of the curve. Sample B's viscosity decreases more rapidly than sample A's, confirming the shear sensitivity of sample B.

The same ramp experiment was performed as viscosity vs. shear rate (Fig. 2). This plot quantifies how the viscosity of the material changes with shear rate. Again, the viscosity of sample B is higher at low shear rates, but both samples decrease in viscosity at the same shear rate. Note that the curves intersect near 10s-1, a common rate for single-point Brookfield viscosity tests. This emphasizes the importance of generating a curve rather than a single point to capture the spectrum of material response.

Yield Stress Phenomena

Yield stress is crucial in determining not only the shelf life of pharmaceutical products, but

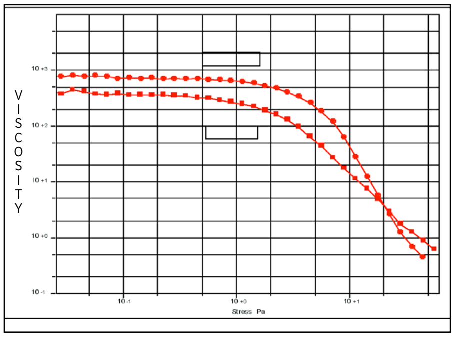

Fig. 1

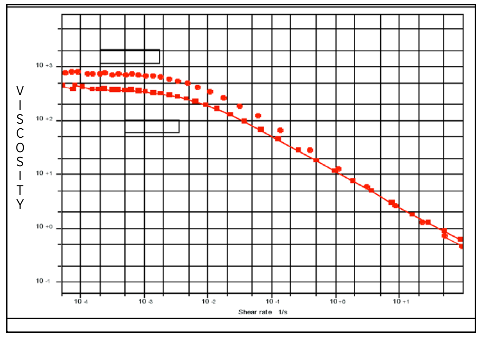

Fig. 2

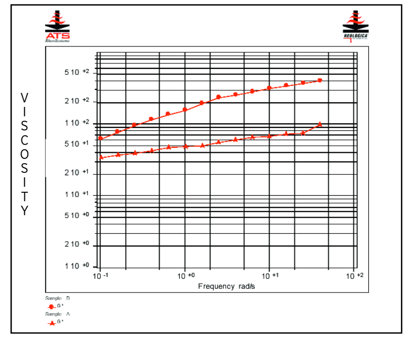

Fig. 3

also ease of application and transfer. Yield stress is defined as the minimum shear stress required to initiate flow and can be measured using a stress-ramp experiment. Yield stress can also be defined as the stress below which a material will not exhibit a fluid-like behavior. This means that subjecting a material to stresses less than the yield stress will lead to a non-permanent deformation or a slow creeping motion during the experiment.

The concept of yield stress—the minimum shear stresses required to cause flow—is just an approximation, as the value depends on the experimental time. Given enough time, all substances will probably flow, no matter how small a load is applied. Generally, the higher the static yield value, the more readily a medium will maintain particles in suspension with minimal sedimentation. Thus, the magnitude of the static yield value may be used as an empirical parameter for controlling the sedimentation on storage and the ease of using or processing a product.

Consumer acceptance of a skin cream depends on its feel when applied to the skin. Such factors, and the stability of a product on the shelf, are governed by its rheological properties. Four samples of hand cream were analyzed using parallel plates with diameters of 20 mm or 30 mm, depending on sample properties. The tests were performed at room temperature.

The results of the yield stress measurement can be directly related to the sensorial properties of the cream. When small stresses are initially applied, it should feel rich, an impression related to high viscosity. At the yield stress, the viscosity starts to decrease rapidly. The lower the yield stress, the easier the cream can be spread on the skin because the yield stress determines the thickness of the cream layer on the skin.

The "mild" and "extra" samples are both hand creams in tubes. The mild sample has the lowest viscosity and yield value, so it will be easy to squeeze out of the tube and spread on the skin. The extra cream is used to protect the hands during work. This must be applied in a thicker layer which requires a higher yield value.

Dynamic Oscillatory Experiments

Although rotational experiments provide information on flow properties such as the yield value, thixotropy and steady shear-flow curve, these are only a part of the complete rheological characterization of a system. Dynamic oscillation testing is a much more powerful tool to reveal the microstructure of a viscoelastic material and is therefore more useful from a practical point of view.

Oscillatory measurements provide information about the structure and elasticity of a material, and can be used to determine storage stability. The oscillation strain sweep measurement is used to find a range of strain where the rheological properties of the samples are independent of the applied strain. These strain values should not be exceeded in further measurements.

For example, when considering an amplitude sweep, sample A has a large linear region, up to an amplitude of 1%, while the linear region of sample B is five times smaller, or 0.2%. This suggests that sample A is a more stable dispersion than sample B. Note also that the modulus in the linear region for sample B is higher by a factor of four, which is not necessarily an indication of suspension stability (Table 1).

Table 1.	LVR [%]	G* [Pa]
Sample A	1	50
Sample B	0.2	200

Frequency Sweep

Once the maximum linear amplitude is determined, a frequency sweep can be performed (Fig. 3). In this test, the amplitude is maintained at a level less than the maximum critical limit and the frequency is modulated in steps. The frequency dependence of the elastic modulus depends greatly on factors such as particle size, distribution and concentration in an emulsion.

Emulsion B shows greater dependence on frequency than emulsion A, despite the fact that the volume fraction of dispersed phase is constant. The difference is in the particle size of the emulsion. Sample B has larger particles and a wider range of particle size. In actual use, sample B was less stable than sample A. Sample B showed syneresis over time in storage stability studies.

Determining the viscoelastic rheological properties as a function of temperature is also important. Many materials are stored at one temperature (25°C) but are applied at body temperature (37°C). Although formulated for the same application, two lip balms, Blistex and Guardian Angel, fall into two different temperature-use ranges when it comes to viscoelastic properties. At 25°C, the samples show similar shear modulus (G') values (stiffness) but differing phase angle. The Blistex sample is less elastic (lower phase angle).

At 37°C, the Blistex sample shows higher modulus values, again with less elasticity. As a result, the Blistex sample will require more force to apply but will adhere to the lips better and provide a softer feel. As the temperature approaches 50°C, the Guardian Angel gel structure is broken and the materials flows like a liquid. Therefore, the product would be unusable if left in sunlight or in a car on a hot summer day.

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